

# Online Research @ Cardiff

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <https://orca.cardiff.ac.uk/id/eprint/126612/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Foxwell, David A, Pradhan, Sara, Zouwail, Soha, Rainer, Timothy H ORCID: <https://orcid.org/0000-0003-3355-3237> and Phillips, Aled O ORCID: <https://orcid.org/0000-0001-9744-7113> 2020. Epidemiology of emergency department acute kidney injury. Nephrology 25 (6) , pp. 457-466. 10.1111/nep.13672 file

Publishers page: <http://dx.doi.org/10.1111/nep.13672>  
<<http://dx.doi.org/10.1111/nep.13672>>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies.

See

<http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



# **Epidemiology of Emergency Department Acute Kidney Injury**

**David A Foxwell, MB BCh<sup>1</sup>**

**Sara Pradhan<sup>1</sup>**

**Soha Zouwail, PhD<sup>2,3</sup>**

**Timothy H Rainer, MD<sup>4</sup>**

**Aled O Phillips, MD<sup>1</sup>**

## **Affiliations**

<sup>1</sup> Institute of Nephrology, University Hospital of Wales, Heath Park, Cardiff, CF14 4XN

<sup>2</sup> Medical Biochemistry Department, University Hospital of Wales, Heath Park, Cardiff, CF14 4XN

<sup>3</sup> Medical Biochemistry Department, School of Medicine, Alexandria University, Egypt

<sup>4</sup> Emergency Medicine Academic Unit, Division of Population Medicine, Cardiff University, CF14 4XN

**Running title:** Acute Kidney Injury in the Emergency Department

## **Word Count**

Text (abstract, introduction, methods, results, discussion, references): 3,843

## **Author Contributions**

D.A.F., S.Z., T.H.R. and A.O.P. designed the study; D.A.F. and S.P. carried out the data collection; D.A.F., T.H.R. and A.O.P. analysed the data; D.A.F. made the figures; D.A.F., S.P.,

S.Z., T.H.R. and A.O.P. drafted and revised the paper; all authors approved the final version of the manuscript.

**Correspondence:** Professor Aled Phillips, Institute of Nephrology, University Hospital of Wales, Heath Park, Cardiff, CF14 4XN. Phone +44 (0)29 2074 8432 [PhillipsAO@cardiff.ac.uk](mailto:PhillipsAO@cardiff.ac.uk)

## Abstract

**Aim:** The epidemiology of Acute Kidney Injury (AKI) diagnosed in the Emergency Department (ED) is poorly described. This study describes the incidence, demographics and outcomes of patients diagnosed with AKI in the ED (ED-AKI).

**Methods:** A prospective cohort study was completed in a University Teaching Hospital, (UK) between April and August 2016. In total 20,421 adult patients attended the ED and had a serum creatinine measurement. The incident ED-AKI patient episodes were compared to a randomly selected cohort of non-AKI ED patients.

**Results:** 572 patients had confirmed eAlert ED-AKI (548 incident cases), [give an](#) incidence [of](#) 2.8% (of all ED attendances). ED-AKI was associated with a 24.4% in patient mortality (non-AKI 3.2%,  $p<0.001$ ) of which 22.3% of deaths occurred within 24-hours and 58% within 7-days. Progression of the admission AKI stage to a higher AKI stage was associated with a 38.8% mortality compared to a 21.4% mortality in those who did not progress ( $p<0.001$ ). In multivariate analysis ED-AKI was an independent risk for mortality (HR, 6.293; 95% CI, 1.887 to 20.790,  $p=0.003$ ). For those discharged from hospital 20.4% of ED-AKI patients re-attend for acute assessment within 30-days post discharge (non-AKI 7.6%,  $p<0.001$ ). At 90-days post discharge 10.0% of ED-AKI patients died (non-AKI 1.4%,  $p<0.001$ ). 12-months post discharge 17.8% of ED-AKI patients developed CKD progression or de-novo CKD (non-AKI 6.0%).

**Conclusion:** ED-AKI is an independent predictor of death. Mortality is predominantly in the early stages of hospital admission, but for those who survive to discharge have significant long-term morbidity and mortality.

**Key Words:** Acute Kidney Injury, Epidemiology, Emergency Departments

## Introduction

Acute Kidney Injury (AKI) is a common medical emergency, complicating 6-18% of all hospital admissions<sup>(1-3)</sup>. There are however, significant variations in the disease phenotype. For example markedly differing mortality has been reported when diagnosed in the community (CA-AKI, 19-26%)<sup>(1, 4-6)</sup>, hospital (HA-AKI, 30-43-%)<sup>(1, 4, 6, 7)</sup> and within the Intensive Care Unit (ICU-AKI, 22-53%)<sup>(8-12)</sup>. In surviving patients long term consequences are well recognised as survivors are at increased risk of de-novo/progressive Chronic Kidney Disease (CKD)<sup>(13)</sup>, End Stage Renal Disease (ESRD)<sup>(14)</sup> and early death<sup>(15)</sup>.

AKI diagnosed in hospital forms the corner stone of a number of in hospital mortality prediction models<sup>(16-18)</sup>. Furthermore, AKI is a major risk factor for long-term mortality<sup>(16)</sup> and impaired neurological outcomes<sup>(19)</sup> following cardio-pulmonary resuscitation. It is unknown if a window of opportunity exists were early identification and aggressive resuscitation can circumvent acute mortality and reduce long-term morbidity.

Our group has previously reported that at a national level CA-AKI contributes to 50% of all AKI events of which half alerted in the Emergency Department, (ED)<sup>(4, 5)</sup>. Despite an annual ED attendance of 23.4 million patients in NHS England <sup>(20)</sup>, very little is known regarding the impact of AKI at the hospital front door, specifically in the ED. To date there have been only two publications investigating AKI in the ED (ED-AKI). Of these, the first described the demographics and risk factors of a small ED-AKI cohort in which AKI was diagnosed on the basis of change in serum creatinine (sCr)<sup>(21)</sup>, and the second involved a larger cohort in which AKI was retrospectively diagnosed from administrative data<sup>(22)</sup>.

ED-AKI represents an important cohort with a significant paucity of data. To inform further research and guide clinical endpoints a detailed description of ED-AKI is required.

In this observational study we compared epidemiology data, risk factors and outcome, of the largest cohort reported to date of adult patients admitted with AKI diagnosed in the ED and compared these to a cohort of randomly selected patients admitted to ED without AKI (non-AKI).

## **Methods**

### **Setting**

This retrospective, single-centre study was conducted over a 17-month period (1<sup>st</sup> April 2016 to 31<sup>st</sup> August 2017) in a University Hospital, Tertiary Referral, Major Trauma and Emergency Care Centre in South Wales (UK) (1080 general beds, 54 ICU beds), serving a population of 445,000. ED attendance was defined as those patients who attended the ED directly and those who were referred to the Acute Medical Assessment Unit and the Acute Surgical Assessment Unit directly from primary care.

### **Electronic Reporting System**

The previously described (and validated) Welsh electronic AKI reporting system (InterSystems TrakCare Lab) was used to identify patients with sCr rises consistent with a diagnosis of AKI<sup>(4, 23)</sup>. The system processes data in real time, automatically comparing sCr levels against historic data (sCr within 365 days) to generate alerts on the basis of the Kidney Disease Improving Global Outcomes (KDIGO) criteria<sup>(24)</sup>.

### **Data Collection**

All adult patients ( $\geq 18$  years of age) who attended the ED and had a sCr test between the 1<sup>st</sup> April and 31<sup>st</sup> August 2016 were eligible for inclusion. Patients were grouped to either ED-AKI or non-AKI dependent upon the generation of an AKI e-alert at ED presentation. Any patient generating an e-alert but at manual data analysis were identified as received a renal transplant, undergoing renal replacement therapy, those who due to incorrect lab-coding had not generated an alert in the ED and any patient self-discharging prior to assessment by a doctor were excluded from the analysis. To inform the true eAlert ED-AKI incidence, all

patients who were admitted or discharged (the total number of renal function tests) were compared to the total number of true positive eAlert ED-AKI episodes to generate the incidence denominator.

A non-AKI control cohort was generated from the incident patients attending the ED with no AKI e-alert by random selection using the random number generating function, Microsoft® Excel® (Ver: 16.11.1), followed by number ordering and selection of the first 600 cases<sup>(25)</sup>.

Following cohort selection all electronic patient records were manually searched by a single nephrologist and demographic, clinical and laboratory data was collated. Pre-existing baseline sCr was defined following review of all historic sCr data. For those with no historic data, admission and post-discharge sCr was reviewed and extrapolated to infer pre-existing baseline. Similarly, all sCr results within 12-months post discharge were trended to describe new baseline. AKI and CKD were defined by KDIGO AKI<sup>(26)</sup> and CKD<sup>(27)</sup> criteria. eGFR was calculated using the Modification of Diet in Renal Disease Study (MDRD) equation<sup>(28)</sup>. Pre-existing CKD was classified as stage 3A-5 only. All sCr results at presentation to the ED from each cohort was compared to baseline to validate the e-alerts. Recovery from AKI was defined as achievement of sCr no longer in keeping with AKI. AKI progression was defined as a peak AKI stage higher than the stage associated with the incident e-alert or for stage 3 alerts an increase  $\geq 50\%$  from the sCr generating the alert<sup>(23)</sup>.

Hospital admission was defined either as those patients who attended the ED but died within 24 hours of admission to hospital or those who attended the ED but were admitted for  $>24$  hours. Recent admission and re-admission within 30-days of incident case was defined as presentation to the ED for acute care or any unscheduled acute hospital admission. Discharge was defined as those who were discharged within 24-hours of ED



presentation and those who were discharged following hospital admission. All discharged patients were followed up for 12 months.

## **Statistics**

Statistical analysis was carried out using SPSS software, version 23 (IBM SPSS, Chicago, IL). Normally distributed data was analysed using t-test. Categorical data were compared using chi-squared test. Data which is non-normally distributed were analysed using Mann-Whitney U test and Kruskal-Wallis test. Continuous variables are described as mean  $\pm$ SD or median and interquartile range (IQR). Multivariate Cox proportional hazard modelling was used to determine the significance of variables on inpatient mortality. Kaplan-Meier survival analysis was performed to assess 90-day mortality. P values  $\leq 0.05$  were considered statistically significant.

## Results

### Patient Cohort

During the five-month cohort identification there were 20,421 ED adult patient contacts who had a sCr test performed. In total 648 ED-AKI e-alerts occurred. Following review of historical sCr results and application of exclusion criteria 572 AKI cases were confirmed, giving an overall ED-AKI incidence of 2.8%. Of the 572 ED-AKI eAlerts, 548 incident cases were identified and entered into analysis (n=24 repeat admissions with ongoing AKI i.e this is the same patients with a second (or more) episode? – the wording needs a little more clarity). In total 600 non-AKI cases were randomly selected from 17,145 incident non-AKI cases. Of these 571 were selected for analysis following application of the exclusion criteria, figure 1.

### Demographic Data

On average ED-AKI patients were 15-years older (70.3 versus 54.7  $p<0.001$ ), a greater proportion were male (54.9% versus 46.2%,  $p=0.004$ ), and nursing or residential home residents at the time of admission (19.5% versus 6.5%,  $p<0.001$ ) compared to the non-AKI cohort. A greater proportion of the ED-AKI cohort had pre-existing CKD (27.6% versus 7.9% non-AKI,  $p<0.001$ ) and a greater proportion of all co-morbid conditions investigated except for Connective Tissue disease/Vasculitis which no difference was demonstrated, table 1.

### ED Contact Data and Investigations

At presentation, a greater proportion of patients in the ED-AKI group had Stage 1 AKI (68.8%), than stage 2 (20.4%) or stage 3 (10.8%). A larger proportion of patients with ED-AKI were admitted to hospital, 83.8% (n=459) compared to 32.9% (n=188,  $p<0.001$ ) of the

control non-AKI ED patients. ED-AKI was most commonly associated with a discharge diagnosis of sepsis, co-existing in 34.1% of cases, table 2.

A greater proportion of patients presenting with ED-AKI had attended the ED in the preceding 30-days compared to the non-AKI group (18.6% versus 13.3%,  $p=0.018$ ). At presentation to the ED, ED-AKI patients were more likely to demonstrate derangement of liver function compared to the non-AKI group; Alanine transaminase (58.2 versus 34.9 U/L,  $p<0.001$ ), Bilirubin (22.0 versus 12.6  $\mu\text{mol/L}$ ,  $p<0.001$ ) and lower albumin (31.1 versus 36.1 g/L,  $p<0.001$ ). The ED-AKI group also had greater increases in inflammatory markers when compared to the non-AKI group, CRP (107.3 versus 29.9 mg/L,  $p<0.001$ ) and WBC ( $12.8$  versus  $9.7 \times 10^9/\text{L}$ ,  $p<0.001$ ).

### **Inpatient Outcomes**

In total 647 patients were admitted to hospital from the ED (across both ED-AKI and non-AKI cohorts). Of the ED-AKI cohort 83.8% were admitted compared to 32.9% of the non-AKI cohort ( $p<0.001$ ). Figure 2 (i) is a detailed flow diagram of the patient journey from admission to discharge or death. Of those admitted to hospital with ED-AKI 2.2% ( $n=10$ ) required inpatient renal replacement therapy (RRT) compared to none in the non-AKI cohort.

Overall the inpatient ED-AKI mortality was 24.4% ( $n=112$ ), compared to 3.2% ( $n=6$ ) in the non-AKI cohort ( $p<0.001$ ). ED-AKI mortality was associated with peak AKI stage reached during admission, stage 1-3 mortality; 17.2%, 27.1% and 40.7% respectively. For those in the admission ED-AKI cohort, 80 progressed to a higher AKI stage during their admission; AKI progression occurred in 53 stage one patients (66.2%), 24 AKI stage two (30%) and 3 AKI stage three patients (3.8%). Mortality in the ED-AKI progression group was 38.8%, compared to 21.4% in the non-progresses ( $p<0.001$ ), Figure 2 (ii). Of those admitted with ED-AKI, 9.8%

(n=45) required Intensive-Care-Unit (ICU) admission during their inpatient stay. Of the total number of ICU admissions, 60% (n=27) occurred in the first 24-hours of presentation to hospital. No patient in the non-AKI cohort was admitted to ICU (table 3). In-patient mortality in those admitted with ED-AKI to the ICU was 31.1%.

22.3% of all deaths in the ED-AKI group occurred within the first 24 hours following presentation at the ED (n=25). 24-hour mortality for each AKI stage at ED presentation was 3.4% in stage one, 6.2% in stage two and 8.5% in stage three, figure 2 (iii). At 72-hours and 7-days following ED-AKI hospital admission the proportion of total mortality was 38.4% and 58.0% respectively. Figure 2 (iv) depicts the distribution of mortality by censoring event day.

By multivariable COX regression for survival analysis ED-AKI increased the odds of mortality (HR, 6.293; 95% CI, 1.887 to 20.790,  $p=0.003$ ). Similarly, advancing age (yrs) was associated with increased odds of mortality (HR, 1.029; 95% CI, 1.012 to 1.047,  $p=0.001$ ), table 4.

### **Post Discharge Short Term Outcomes**

Of the total 548 subjects in the ED-AKI cohort, 89 were discharged direct from the ED and 459 were admitted to hospital. In total 436 ED-AKI patients were discharged from hospital following a diagnosis of ED-AKI. At 30-days the hospital re-admission rate for the discharged ED-AKI group was 20.4% compared to 7.6% in the non-AKI group,  $p<0.001$ .

At 90-days post hospital discharge 43 deaths (10.0%) in the ED-AKI group occurred compared to 8 deaths (1.4%) in the non-AKI group ( $p<0.001$ ). Figure 3 shows the Kaplan-Meier Survival analysis at 90 days for ED-AKI vs Non-AKI (Figure 3, i) and for AKI stage on admission to hospital relative to non-AKI, figure 3 (ii).

### **Post Discharge One Year Outcomes**

At 12-months, 81.7% (n=356) of those with ED-AKI who survived to discharge were alive, compared to 95.9% (n=542) of the non-AKI cohort ( $p<0.001$ ). Of these, 326 (91.6 %) patients with ED-AKI and 470 (86.7%) of the non-AKI cohort had sufficient clinical data to assess for biochemical evidence of CKD. Mean sCr data was higher in the ED-AKI cohort than the non-AKI cohort at 12-months, (106.3  $\mu\text{mol/L}$  versus 80.6  $\mu\text{mol/L}$ ,  $p<0.001$ ), figure 3 (iii). Evidence of pre-existing CKD progression occurred in 8.9% (n=29) of the ED-AKI cohort compared to 3.4% (n=16) of the non-AKI cohort, ( $p=0.005$ ), figure 3 (iv). Furthermore, de-novo CKD was identified in 8.9% (n=29) of the ED-AKI group compared to 2.6% (n=12) of the non-AKI group, ( $p=0.006$ ), figure 3 (v). Of the ten ED-AKI patients who required inpatient RRT eight recovered renal function to a level sufficient to negate the need for RRT and two were discharged with ongoing RRT. At 12-months three patients in the ED-AKI cohort progressed to end-stage renal failure (ESRF) requiring RRT compared to no patients requiring RRT in the non-AKI cohort.

## Discussion

To the best of our knowledge this is the largest non-administrative epidemiology study of adult ED-AKI patients to-date. In this study of 20,421 consecutive adult patients attending and undergoing a sCr test in the ED we identified 572 eAlert ED-AKI episodes, giving an ED-AKI incidence of 2.8%. The inclusion of all patients attending the ED (both admitted and discharged) in the incidence calculation allows a more comprehensive estimate of ED-AKI incidence that previous studies which focus solely on admitted patients would over-estimate.

Our ED-AKI population was older, more likely to be male and reside in a residential/nursing facility on presentation to the ED when compared to a randomly selected group of non-AKI ED attendees. Consistent with the finding that AKI occurs in an older population our study demonstrated AKI patients are more likely to have multiple co-morbidities, including pre-existing CKD, cardio-vascular disease, hypertension, dementia, malignancy, liver and lung disease. These findings are similar to a smaller epidemiology ED-AKI study<sup>(21)</sup> and mirrors observations in HA-AKI<sup>(2, 7)</sup> and ICU-AKI<sup>(10, 11)</sup> cohorts.

In those admitted to hospital, the ED-AKI mortality was 24.4% versus 3.2% in the non-AKI cohort. In the first 24 hours of ED-AKI presentation mortality was 4.6%, which attributed to 22.3% of the total ED-AKI mortality. The proportion of the total ED-AKI mortality increased to 38.4% and 58% at 72-hrs and 7-days respectively. Patients who progressed to a higher AKI stage during their hospital admission had a greater in-hospital mortality, (38.8% versus 21.4% in the non-progresses). To our knowledge we are the first group to describe a high acute mortality within the early phases of ED-AKI presentation. A small ED-AKI cohort (n=90) examined by Scheuermeyer et al 2017, reported the proportion of hospital admissions to be 65.5%, and a 30-day mortality of 18.6%<sup>(21)</sup>. The higher inpatient mortality of our study may

reflect the larger sample size and more comprehensive mechanism of identifying all cases. When comparing to other AKI studies in differing clinical settings, in hospital mortality has been reported ranging from 20-52%<sup>(1, 6)</sup>.

ED-AKI patients were more likely to present to acute hospital services in the preceding 30-days (18.6% vs 13.3%,  $p < 0.018$ ) and re-attend for acute assessment 30-days post discharge (20.4% vs 7.6%,  $p < 0.001$ ). At 90-days 10.1% of ED-AKI discharges died (non-AKI 1.4%). Acedillo et al, 2017 conducted a large ED-AKI population based administrative study in Canada, reporting a 16% readmission and 8% mortality at 30-days<sup>(29)</sup>. In contrast to our data on all adults >18yrs of age, this study only examined patients  $\geq 40$ yrs of age and excluded those ED patients who died on arrival or during the ED visit.

At 12-months those discharged following an ED-AKI episode were more likely to develop CKD progression, 8.9% (non-AKI 3.4%) and de-novo CKD, 8.9% (non-AKI 2.6%). The association between de-novo CKD and CKD progression has been described in other AKI populations<sup>(30-32)</sup> and confirmed by meta-analysis<sup>(33)</sup>. To our knowledge this is the first study of ED-AKI patients examining long term renal outcomes.

Although our study is of a large well-characterised cohort it has limitations. As a single centre study, extrapolation to other health care systems may not be appropriate owing to subtle health-care differences. The use of historical biochemistry to infer AKI falls outside the strict definition of KDIGO AKI which relies on a sCr rise within 48 hours. Our study aimed to limit this impact by reviewing all retrospective and prospective sCr results to validate the e-alert. Our study did not use urine output to diagnosis AKI, but, in the context of the ED where urine outputs are often unavailable the extrapolation of historic sCr data to infer AKI may be the most appropriate. Owing to CKD stage 1 and 2 relying upon abnormal urinalysis and/or structural pathology for diagnosis, CKD 1 and 2 could not be reliably inferred so our study

may underestimate CKD incidence. We were unable to provide data concerning medication prescription at the time of ED presentation due to insufficient retrospective data linkage to primary care. I think this is where you can touch eAlerts not being able to pick up patients with no previous results? Might then be a way later (if a reviewer pick up) to address the reviewers comments – so just a limitation to eAlerts – have a think – not really bothered either way to be honest!!

In conclusion, we present the largest non-administrative epidemiology study of ED-AKI patients to date. ED-AKI is an independent risk for death particularly in the early stages of admission. ED-AKI patients more often access acute medical services before the incident event and after recovery and discharge to the community. Following discharge ED-AKI is associated with a heightened mortality and adverse long term renal outcomes. How access to healthcare, patient education and enhanced follow-up will impact ED-AKI acutely and chronically is unknown but further studies are required.



### **Acknowledgments and Disclosure of Financial Interests**

We declare no financial interest. Disclosures: None.

## References

1. Wonnacott A, Meran S, Amphlett B, Talabani B, Phillips A. Epidemiology and outcomes in community-acquired versus hospital-acquired AKI. *Clin J Am Soc Nephrol*. 2014;9(6):1007-14.
2. Xu X, Nie S, Liu Z, et al. Epidemiology and Clinical Correlates of AKI in Chinese Hospitalized Adults. *Clin J Am Soc Nephrol*. 2015;10(9):1510-8.
3. Zeng X, McMahon GM, Brunelli SM, Bates DW, Waikar SS. Incidence, outcomes, and comparisons across definitions of AKI in hospitalized individuals. *Clin J Am Soc Nephrol*. 2014;9(1):12-20.
4. Holmes J, Rainer T, Geen J, et al. Acute Kidney Injury in the Era of the AKI E-Alert. *Clin J Am Soc Nephrol*. 2016;11(12):2123-31.
5. Holmes J, Allen N, Roberts G, Geen J, Williams JD, Phillips AO. Acute kidney injury electronic alerts in primary care - findings from a large population cohort. *QJM*. 2017;110(9):577-82.
6. Hsu CN, Lee CT, Su CH, et al. Incidence, Outcomes, and Risk Factors of Community-Acquired and Hospital-Acquired Acute Kidney Injury: A Retrospective Cohort Study. *Medicine (Baltimore)*. 2016;95(19):e3674.
7. Jurawan N, Pankhurst T, Ferro C, et al. Hospital acquired Acute Kidney Injury is associated with increased mortality but not increased readmission rates in a UK acute hospital. *BMC Nephrol*. 2017;18(1):317.
8. Holmes J, Roberts G, Geen J, et al. Utility of electronic AKI alerts in intensive care: A national multicentre cohort study. *J Crit Care*. 2018;44:185-90.

9. Fuhrman DY, Kane-Gill S, Goldstein SL, Priyanka P, Kellum JA. Acute kidney injury epidemiology, risk factors, and outcomes in critically ill patients 16-25 years of age treated in an adult intensive care unit. *Annals of intensive care*. 2018;8(1):26.
10. Odutayo A, Adhikari NK, Barton J, et al. Epidemiology of acute kidney injury in Canadian critical care units: a prospective cohort study. *Can J Anaesth*. 2012;59(10):934-42.
11. Hoste EA, Bagshaw SM, Bellomo R, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. *Intensive Care Med*. 2015;41(8):1411-23.
12. Abd ElHafeez S, Tripepi G, Quinn R, et al. Risk, Predictors, and Outcomes of Acute Kidney Injury in Patients Admitted to Intensive Care Units in Egypt. *Sci Rep*. 2017;7(1):17163.
13. Arias-Cabrales C, Rodriguez E, Bermejo S, et al. Short- and long-term outcomes after non-severe acute kidney injury. *Clin Exp Nephrol*. 2018;22(1):61-7.
14. Ishani A, Xue JL, Himmelfarb J, et al. Acute kidney injury increases risk of ESRD among elderly. *J Am Soc Nephrol*. 2009;20(1):223-8.
15. Silver SA, Harel Z, McArthur E, et al. Causes of Death after a Hospitalization with AKI. *J Am Soc Nephrol*. 2018;29(3):1001-10.
16. Geri G, Guillemet L, Dumas F, et al. Acute kidney injury after out-of-hospital cardiac arrest: risk factors and prognosis in a large cohort. *Intensive Care Med*. 2015;41(7):1273-80.
17. Edwards FH, Cohen DJ, O'Brien SM, et al. Development and Validation of a Risk Prediction Model for In-Hospital Mortality After Transcatheter Aortic Valve Replacement. *JAMA cardiology*. 2016;1(1):46-52.
18. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med*. 1985;13(10):818-29.

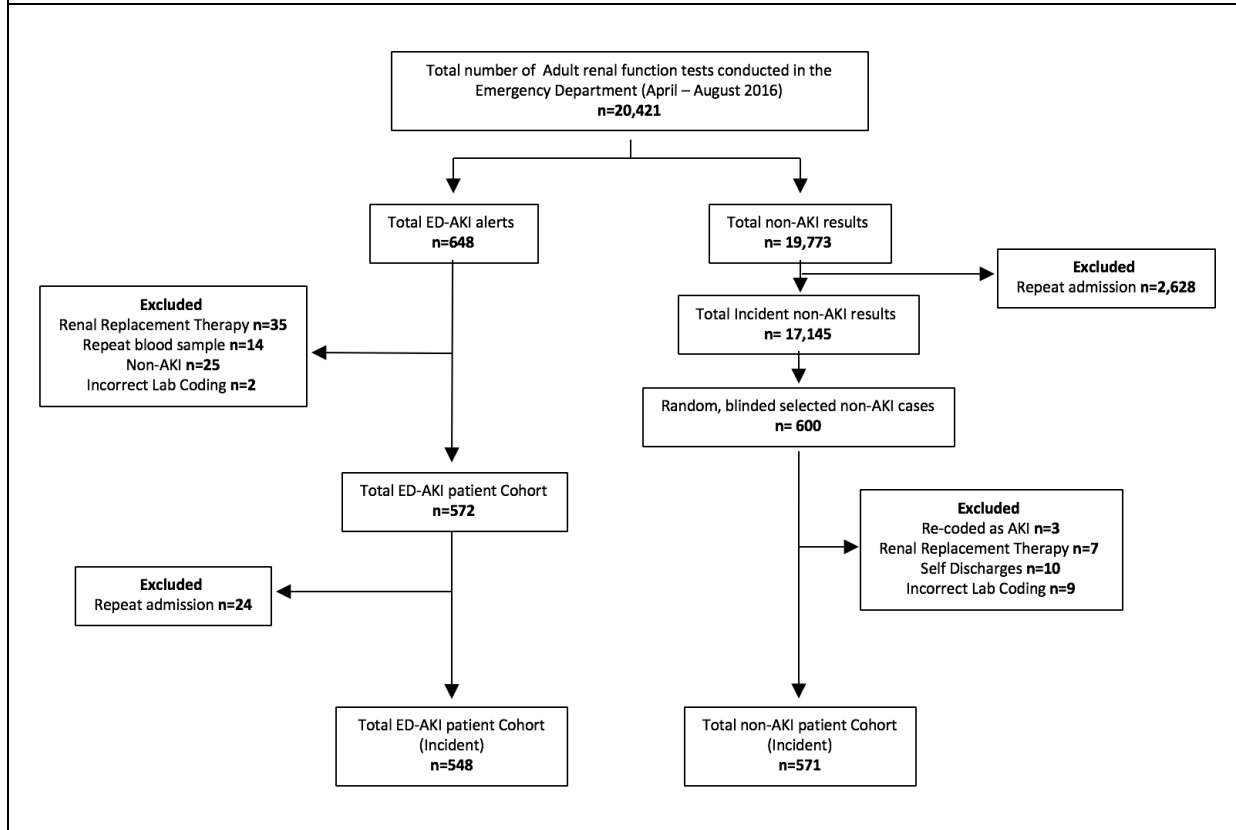
19. Storm C, Krannich A, Schachtner T, et al. Impact of acute kidney injury on neurological outcome and long-term survival after cardiac arrest - A 10year observational follow up. *J Crit Care*. 2018;47:254-9.
20. NHS Digital. Hospital Accident and Emergency Activity, 2016-17 2017 [Available from: <https://digital.nhs.uk/catalogue/PUB30112>].
21. Scheuermeyer FX, Grafstein E, Rowe B, et al. The Clinical Epidemiology and 30-Day Outcomes of Emergency Department Patients With Acute Kidney Injury. *Canadian journal of kidney health and disease*. 2017;4:2054358117703985.
22. Acedillo RR, Wald R, McArthur E, et al. Characteristics and Outcomes of Patients Discharged Home from an Emergency Department with AKI. *Clin J Am Soc Nephrol*. 2017.
23. Holmes J, Roberts G, Meran S, Williams JD, Phillips AO. Understanding Electronic AKI Alerts: Characterization by Definitional Rules. *Kidney international reports*. 2017;2(3):342-9.
24. Kellum JA, Lameire N. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). *Crit Care*. 2013;17(1):204.
25. Altman DG, Bland JM. How to randomise. *BMJ*. 1999;319(7211):703-4.
26. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract*. 2012;120(4):c179-84.
27. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3:1-150.
28. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999;130(6):461-70.

29. Silver SA, Harel Z, McArthur E, et al. 30-Day Readmissions After an Acute Kidney Injury Hospitalization. *Am J Med.* 2017;130(2):163-72.e4.
30. Bucaloiu ID, Kirchner HL, Norfolk ER, Hartle JE, 2nd, Perkins RM. Increased risk of death and de novo chronic kidney disease following reversible acute kidney injury. *Kidney Int.* 2012;81(5):477-85.
31. Hsu CY, Chertow GM, McCulloch CE, Fan D, Ordonez JD, Go AS. Nonrecovery of kidney function and death after acute on chronic renal failure. *Clin J Am Soc Nephrol.* 2009;4(5):891-8.
32. Soto K, Campos P, Pinto I, et al. The risk of chronic kidney disease and mortality are increased after community-acquired acute kidney injury. *Kidney Int.* 2016;90(5):1090-9.
33. Coca SG, Singanamala S, Parikh CR. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. *Kidney Int.* 2012;81(5):442-8.

## **Acknowledgements**

We have no acknowledgments

**Figure 1:** Inclusion and Exclusion criteria used to define the ED-AKI and the non-AKI cohorts



**Table 1:** Demographic Data: Emergency Department AKI versus Non-AKI

Variable	ED-AKI (n=548)	Non-AKI (n=571)	P value
Age (yr), mean $\pm$ SD	70.3 $\pm$ 18.0	54.7 $\pm$ 21.8	<0.001
Men, % (n)	54.9 (301)	46.2 (264)	0.004
Nursing/Residential Home Resident, % (n)	19.5 (107)	6.5 (37)	<0.001
Mean Creatinine (pre-admission) $\pm$ SD ( $\mu$ mol/L)	94.5 $\pm$ 42.7	77.0 $\pm$ 26.8	<0.001
Baseline eGFR (pre-admission), mean $\pm$ SD	81.0 $\pm$ 31.0	101.7 $\pm$ 29.0	<0.001
Pre-admission CKD 3a-5, % (n)	27.6 (151)	7.9 (45)	<0.001
Stage 3A	15.9 (87)	4.7 (27)	
Stage 3B	8.8 (48)	2.1 (12)	
Stage 4	2.5 (14)	0.9 (5)	
Stage 5	0.4 (2)	0.2 (1)	
<b>Comorbid conditions, % (n) <sup>†,‡</sup></b>			
Peripheral Vascular Disease	5.3 (29)	1.4 (8)	0.003
Cardio Vascular Disease	35.8 (196)	22.8 (130)	<0.001
Hypertension	52.6 (288)	30.1 (172)	<0.001
Diabetes	28.1 (154)	10.2 (58)	<0.001
Hyperlipidaemia	32.7 (179)	17.7 (101)	<0.001
Connective Tissue disease/vasculitis	5.1 (28)	2.6 (15)	0.420
Lung Disease	16.6 (91)	6.8 (39)	<0.001
Liver Disease	5.3 (29)	0.9 (5)	<0.001
Dementia	10.8 (59)	4.0 (23)	<0.001
Active Malignancy	15.5 (85)	6.8 (39)	<0.001

<sup>†</sup> Peripheral Vascular Disease defined as symptomatic claudication and documented clinical/radiological evidence of vascular disease and/or received non-coronary angioplasty, vascular graft or amputation. Cardio Vascular Disease defined as known Angina, Myocardial Infarction, Heart Failure, Stroke or Transient Ischaemic Attack. Hypertension defined as present if requiring medical treatment. Diabetes included both type 1 or type 2 diabetes. Hyperlipidaemia defined as those requiring lipid modifying agents. Connective Tissue disease/Vasculitis defined as known Vasculitis, Rheumatoid Arthritis, Systemic Lupus Erythematosus, Systemic Sclerosis or Polymyositis. Lung disease defined as confirmed COPD, Intestinal Lung Disease or Pulmonary Hypertension. Liver disease includes those with known Cirrhosis. Dementia defined as diagnosed dementia of any aetiology. Active malignancy includes those with palliative malignancy, undergoing active treatment or surveillance.

<sup>‡</sup> P-values were adjusted for multiple tests through Bonferroni adjustment; multiplication of unadjusted p-value by number of tests (n=10)



**Table 2:** Patient Contact Data: Emergency Department AKI versus Non-AKI

Variable	ED-AKI (n=548)	Non-AKI (n=571)	P value
<b>Previous hospital admission, % (n)<sup>†</sup></b>	18.6 (102)	13.3 (76)	0.018
<b>Laboratory Indexes on admission, mean <math>\pm</math>SD (n)</b>			
Creatinine (umol/L)	190.5 $\pm$ 117.6 (548)	78.09 $\pm$ 27.9 (571)	<0.001
Sodium (mmol/L)	135.3 $\pm$ 6.6 (548)	137.6 $\pm$ 4.0 (571)	<0.001
Albumin (g/L)	31.1 $\pm$ 6.7 (511)	36.1 $\pm$ 6.0 (499)	<0.001
Alanine transaminase (U/L)	58.2 $\pm$ 161.0 (499)	34.9 $\pm$ 90.9 (486)	0.005
Bilirubin (umol/L)	22.0 $\pm$ 43.5 (499)	12.6 $\pm$ 19.0 (487)	<0.001
C-Reactive Protein (mg/L)	107.3 $\pm$ 114.9 (480)	29.9 $\pm$ 54.9 (411)	<0.001
White Blood Cell ( $10^9$ /L)	12.8 $\pm$ 7.2 (544)	9.7 $\pm$ 4.6 (559)	<0.001
<b>AKI stage at ED contact, % (n)</b>			
No-AKI	/	100 (571)	
Stage 1 AKI	68.8 (377)	/	
Stage 2 AKI	20.4 (112)	/	
Stage 3 AKI	10.8 (59)	/	
<b>Hospital Admission, % (n)<sup>‡</sup></b>	83.8 (459)	32.9 (188)	<0.001
<b>Discharge Diagnosis, % (n)<sup>§</sup></b>			
Sepsis	34.1 (187)	13.5 (77)	<0.001
Trauma	4.7 (26)	11.4 (65)	<0.001
Surgical Emergency	6.9 (38)	3.7 (21)	0.290
Cardiovascular	10.8 (59)	9.8 (56)	1.00
Gastrointestinal medical	13.1 (72)	6.3 (36)	0.002
Urological obstruction	10.4 (57)	1.2 (7)	<0.001
Malignancy	2.6 (14)	1.9(11)	1.00
Diabetes	5.5 (30)	0.2 (1)	<0.001
Medical/Surgical general	4.6 (25)	48.5 (277)	<0.001
Unknown	7.3 (40)	3.5 (20)	0.10

Sepsis defined as clinical reporting in discharge summaries. Trauma was defined as musculoskeletal injury requiring medical intervention or observation. Surgical emergency was defined as ruptured abdominal viscera, abdominal catastrophe or any emergency surgical intervention. Cardiovascular defined as acute coronary syndrome, angina or cerebrovascular event. Gastrointestinal medical defined as disturbance in gut activity requiring medical support. Urological obstruction defined as bladder outflow obstruction or hydronephrosis as primary cause for admission. Diabetes defined as diabetic complication requiring medical intervention. Medical/Surgical general defined as non-sepsis related infections, surgical pathology not requiring an acute operation.

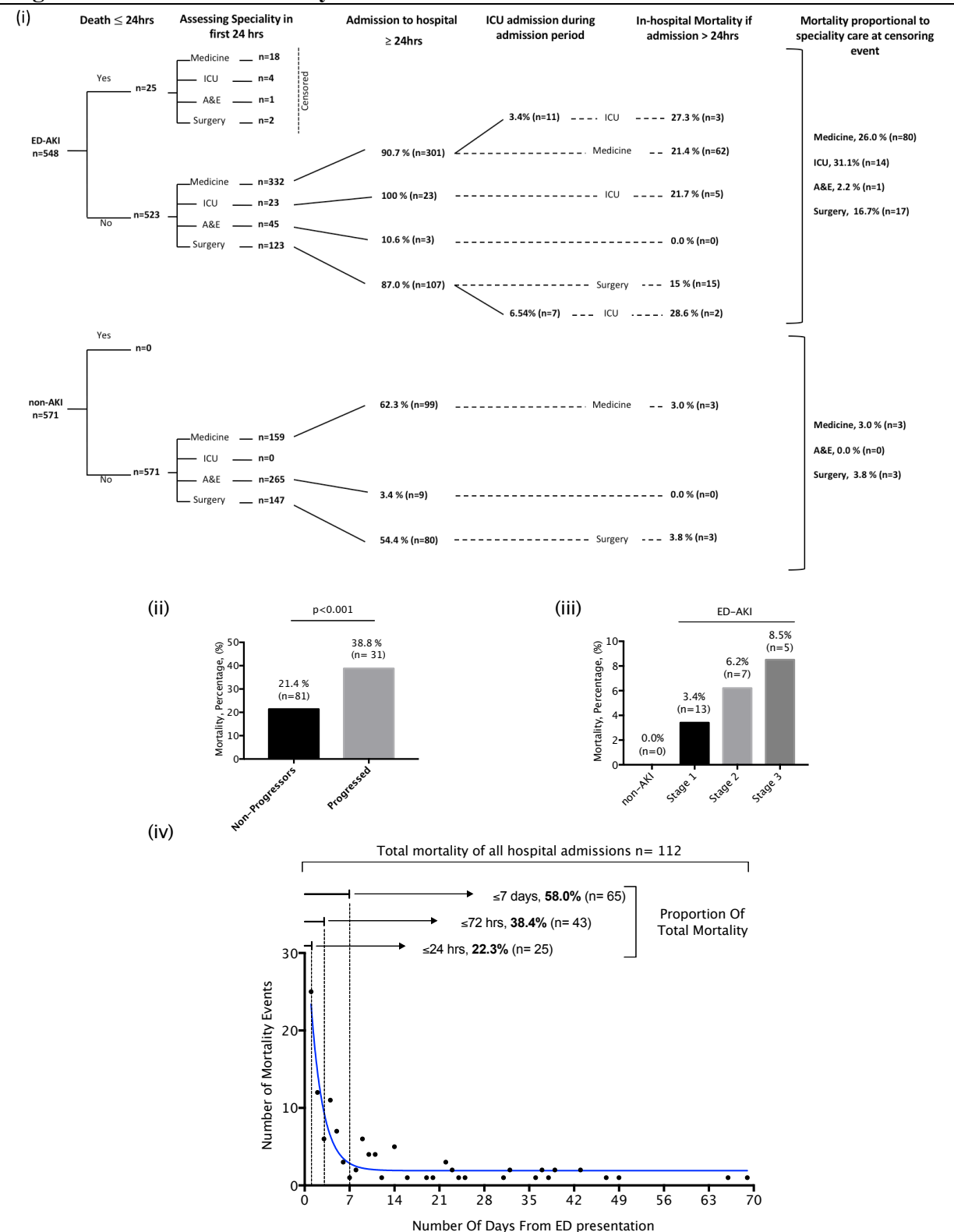
<sup>†</sup> Previous hospital admission defined as any unscheduled admission to hospital within 30-days prior to incident event. <sup>‡</sup> Hospital admission defined as the sum of those who died  $\leq$  24hrs following admission and those who were admitted for >24 hrs. <sup>§</sup> Discharge diagnosis was collated following review of all discharge summaries. Chi-squared test was performed and p-values were adjusted for multiple tests through Bonferroni adjustment; multiplication of unadjusted p-value by number of tests (n=10).

**Table 3:** In hospital Outcomes for those admitted to hospital

<b>Variable</b>	<b>ED-AKI (n=459)</b>	<b>Non-AKI (n=188)</b>	<b>P value</b>
<b>Median length of hospital admission (IQR) (d)</b>	7.0 (3-16)	6.0 (3-13.75)	0.246
<b>ICU admission % (n)</b>	9.8 (45)	/	
<b>Median length of ICU admission (IQR) (d)</b>	5.0 (3-14)	/	
<b>AKI event during admission, % (n)</b>	100.0 (459)	10.6 (20)	<0.001
<b>Peak AKI stage during admission, % (n)</b>			
No-AKI	/	89.4 (168)	
Stage 1 AKI	54.5 (250)	8.0 (15)	
Stage 2 AKI	25.7 (118)	2.1 (4)	
Stage 3 AKI	19.8 (91)	0.5 (1)	
<b>In-hospital mortality, % (n)</b>	24.4 (112)	3.2 (6)	<0.001
<b>Mortality in ICU, % (n)<sup>b</sup></b>	31.1 (14)	/	/
<b>Mortality relative to Peak AKI stage during admission, % (n)</b>			
No-AKI	/	3.0 (5)	
Stage 1 AKI	17.2 (43)	6.7 (1)	
Stage 2 AKI	27.1 (32)	/	
Stage 3 AKI	40.7 (37)	/	

Hospital admission defined as the sum of those who died  $\leq$  24hrs following admission and those who were admitted for >24 hrs. Peak AKI stage defined using the highest sCr result recorded during admission which was then staged according to KDIGO AKI criteria.

**Figure 2: The Patient Journey**



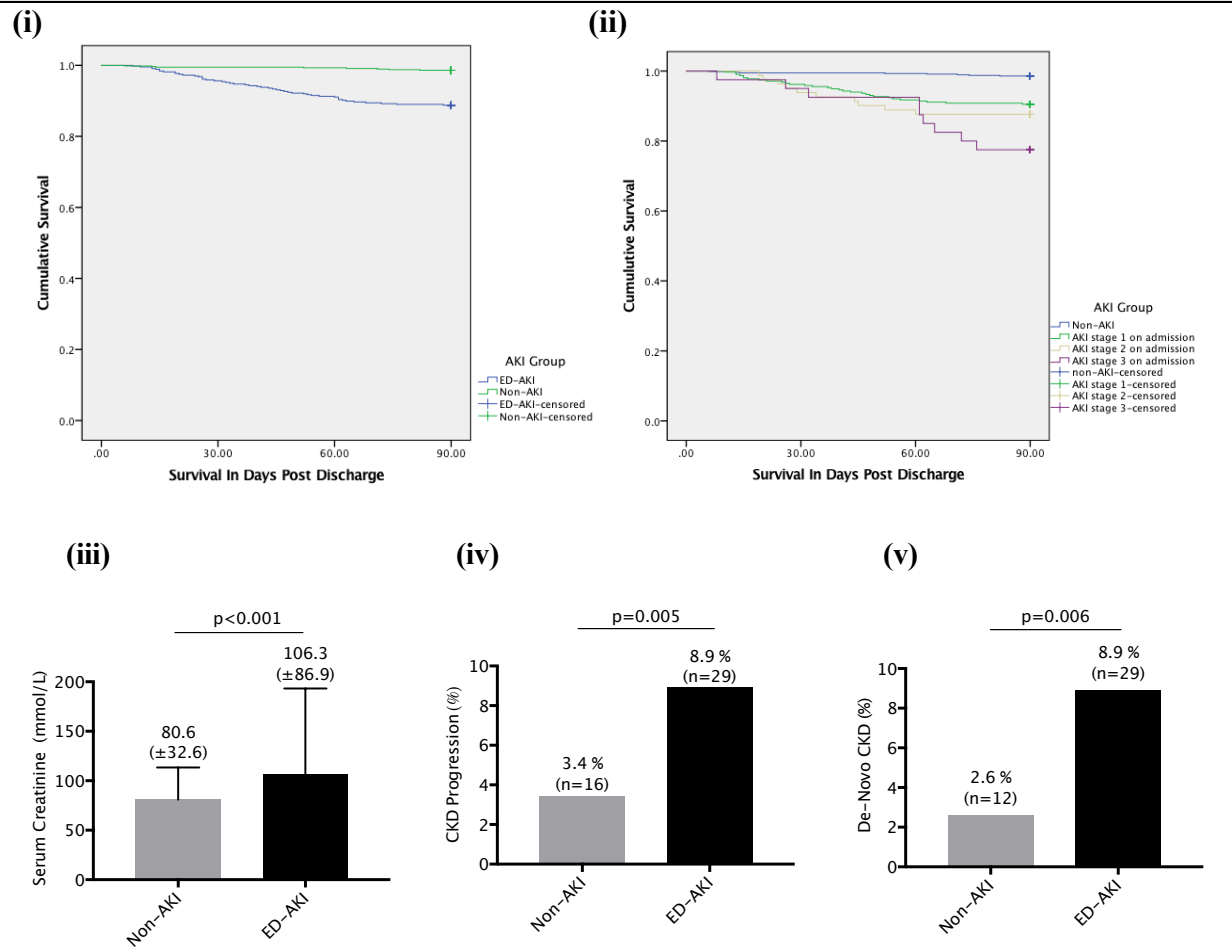
In total 118 patients died in both cohorts, ED-AKI (n=112) and non-AKI (n=6). The patient journey from admission to discharge is described in image (i). The proportion of the total mortality for the ED-AKI cohort occurring in the first 24 hours of admission was 22.3% (n=25), image (iii). Of these the greatest proportion of deaths occurred in the group with stage-3 AKI on admission (n=5, 8.5%), image (iii). Progression of the initial presenting ED-AKI stage to a higher AKI stage occurred in 80 patients of which inpatient mortality was 38.8% (n=31). This compared to 379 patients who did not progress to a higher AKI stage of which 21.4% (n=81) died during admission. The mortality relative to AKI progression is shown image (ii).

**Table 4:** Univariate and multivariate Cox regression analysis of prognostic factors for in hospital survival

Variable	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
ED-AKI versus non-AKI	7.073	3.109-16.091	<b>&lt;0.001*</b>	6.293	1.887-20.790	<b>0.003*</b>
Age, yrs	1.032	1.018-1.045	<b>&lt;0.001*</b>	1.029	1.012-1.047	<b>0.001*</b>
NH/RH Resident	1.628	1.088-2.436	<b>0.018*</b>	1.182	0.717-1.946	0.512
Albumin	0.927	0.901-0.954	<b>&lt;0.001*</b>	0.946	0.907-0.986	<b>0.008*</b>
ALT	1.001	1.000-1.002	<b>0.006*</b>	1.001	1.000-1.001	0.218
C-Reactive Protein	1.002	1.000-1.003	<b>0.009*</b>	1.000	0.998-1.002	0.938
White Blood Cell count	1.038	1.017-1.059	<b>&lt;0.001*</b>	1.016	0.990-1.043	0.223
CKD evidence	1.6112	1.105-2.352	<b>0.013*</b>	1.089	0.668-1.776	0.733
CT disease/vasculitis	2.651	1.456-4.826	<b>0.001*</b>	1.120	0.514-2.441	0.776
Length of Stay, days	0.808	0.764-0.855	<b>&lt;0.001*</b>	0.004	0.000-0.083	<b>&lt;0.001*</b>
Dementia	1.101	0.692-1.752	0.684			
Malignancy	1.530	0.970-2.414	0.067			
ICU admission	1.257	0.717-2.204	0.452			
Male vs. female	0.967	0.674-1.388	0.857			
Sodium	1.026	0.999-1.054	0.061			
Bilirubin	1.002	0.999-1.005	0.252			
Peripheral Vascular Disease	1.021	0.497-2.100	0.954			
Cardiovascular Disease	0.856	0.589-1.243	0.413			
Hypertension	0.889	0.618-1.277	0.524			
Diabetes	0.834	0.539-1.290	0.415			
Hyperlipidaemia	0.660	0.436-1.001	0.051			
Lung Disease	0.684	0.571-1.445	0.684			
Liver Disease	1.457	0.779-2.726	0.239			

Cox regression for survival analysis was used to investigate the association between survival time of those admitted to hospital and predictor variables. The influence of demographic, biochemical, haematological, co-morbid conditions, ICU admission and length of hospital stay was used to inform variables which convey risk/protection. Analysis datasets included only those who were defined as being admitted to hospital. The listed variables were initially investigated by univariate analysis to inform those of statistical significance which were then used in the model of multivariable analysis.  $P < 0.05$  was denoted as statistically significant and are bolded and starred to facilitate easy of reference. Hazard Ratio (HR)  $< 1$  corresponds to a reduction in hazard and  $> 1$  an increase in hazard.

**Figure 3: Short and Long-Term Outcomes**



Kaplan-Meier survival Analysis for all-cause mortality at 90-days post discharge for ED-AKI versus non-AKI is shown in image (i). The survival distributions for ED-AKI versus non-AKI were statistically different  $\chi^2(2) = 44.629$ ,  $p < 0.001$ . Analysis of AKI stage on admission was also completed, image (ii). The survival distributions by AKI stage on admission were statistically significant  $\chi^2(2) = 56.386$ ,  $p < 0.001$ . At 12-months 326 patients of the ED-AKI and 470 of the non-AKI cohort had sufficient clinical data to infer new baseline sCr. Image (iii) depicts the mean serum creatinine of patients 12-months following discharge, data is displayed as mean ( $\pm$ SD). The incidents of CKD progression at 12 months is displayed in image (iv). CKD progression is defined as pre-ED attendance baseline CKD 3A-4 progressing to a higher CKD stage and/or eGFR at baseline (in only those with CKD 3A-5) or a reduction in eGFR by  $\geq 5$ ml/min over 12 months. Data is displayed as percentage (n). The proportion of patients developing De-Novo CKD at 12-months post discharge is presented in image (v). De-Novo CKD is defined as a new diagnosis of CKD 3A-5 12-months post hospital discharge. Data is displayed as percentage (n).